Amendments to the Claims

Kindly amend claims 38, 49, 81 and 84 as follows.

STATUS OF THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the above-referenced application.

1. (withdrawn) A composition comprising: an RNAi-inducing entity, wherein the RNAi-inducing entity is targeted to a target transcript; and a delivery agent selected from the group consisting of: cationic polymers, modified cationic polymers, peptide molecular transporters, surfactants suitable for introduction into the lung, liposomes, non-cationic polymers, modified non-cationic polymers, bupivacaine, and chloroquine.

2. (withdrawn) The composition of claim 1, wherein the delivery agent comprises a delivery-enhancing moiety to enhance delivery to a cell of interest.

3. (withdrawn) The composition of claim 2, wherein the delivery-enhancing moiety comprises an antibody, antibody fragment, or ligand that specifically binds to a molecule expressed by the cell of interest.

4. (withdrawn) The composition of claim 3, wherein the cell of interest is a respiratory epithelial cell.

5. (withdrawn) The composition of claim 2, wherein the delivery-enhancing moiety comprises a moiety selected to reduce degradation, clearance, or nonspecific binding of the delivery agent.

6. (withdrawn) The composition of claim 1, wherein a disease or clinical condition, or a symptom thereof, is associated with excessive expression or inappropriate expression of the target transcript or inappropriate or excessive functional activity of a polypeptide encoded by the target transcript.

7. (withdrawn) The composition of claim 1, wherein the RNAi-inducing entity comprises an siRNA.

8. (withdrawn) The composition of claim 1, wherein the RNAi-inducing entity comprises an shRNA.

9. (withdrawn) The composition of claim 1, wherein the RNAi-inducing entity comprises a lentivirus.

10. (withdrawn) The composition of claim 1, wherein the RNAi-inducing entity comprises an RNAi-inducing vector.

11. (withdrawn) The composition of claim 10, wherein: the vector comprises a nucleic acid comprising a promoter for RNA polymerase III.

12. (withdrawn) The composition of claim 11, wherein: the promoter is a U6 or H1 promoter.

13. (withdrawn) The composition of claim 1, wherein the RNAi-inducing entity comprises a viral vector.

14. (withdrawn) The composition of claim 1, wherein the RNAi-inducing entity comprises a lentiviral vector.

15. (withdrawn) The composition of claim 1, wherein the RNAi-inducing entity comprises a DNA vector.

16. (withdrawn) The composition of claim 1, wherein: the RNAi-inducing entity is an siRNA or shRNA targeted to a target transcript or an RNAi-inducing vector whose presence within a cell results in production of an siRNA or shRNA targeted to a target transcript, wherein the siRNA or shRNA comprises a portion that is perfectly complementary to a region of the target transcript, wherein the portion is at least 15 nucleotides in length.

17. (withdrawn) The composition of claim 1, wherein: the RNAi-inducing entity is an siRNA or shRNA targeted to a target transcript or an RNAi-inducing vector whose presence within a cell results in production of an siRNA or shRNA targeted to a target transcript, wherein the siRNA or shRNA comprises a portion that is perfectly complementary to a region of the target transcript, wherein the portion is approximately 19 nucleotides in length.

18. (withdrawn) The composition of claim 1, wherein: the RNAi-inducing entity is an siRNA or shRNA targeted to a target transcript or an RNAi-inducing vector whose presence within a cell results in production of an siRNA or shRNA targeted to a target transcript, wherein the siRNA or shRNA comprises a portion that is perfectly complementary to a portion of the target transcript, with the

exception of three or fewer nucleotides, wherein the portion is at least 15 nucleotides in length.

19. (withdrawn) The composition of claim 1, wherein: the RNAi-inducing entity is an siRNA or shRNA targeted to a target transcript or an RNAi-inducing vector whose presence within a cell results in production of an siRNA or shRNA targeted to a target transcript, wherein the siRNA or shRNA comprises a portion that is perfectly complementary to a portion of the target transcript, with the exception of three or fewer nucleotides, wherein the portion is approximately 19 nucleotides in length.

20. (withdrawn) The composition of claim 1, further comprising at least one pharmaceutically acceptable diluent, excipient, or carrier.

21. (canceled)

22. (canceled)

23. (withdrawn) The composition of claim 1, wherein the delivery agent is selected from the group consisting of cationic polymers and modified cationic polymers.

24. (withdrawn)The composition of claim 23, wherein the cationic polymer is selected from the group consisting of polylysine, polyarginine, polyethyleneimine, polyvinylpyrrolidone, chitosan, and poly(.beta.-amino ester) polymers.

25. (withdrawn) The composition of claim 24, wherein the cationic polymer is polyethyleneimine.

26. (withdrawn) The composition of claim 24, wherein the cationic polymer is selected from the group consisting of poly(□-amino ester) polymers.

27. (withdrawn) The composition of claim 24, wherein the modified cationic polymer incorporates a modification selected to reduce the cationic nature of the polymer.

28. (withdrawn) The composition of claim 27, wherein the modification comprises substitution with a group selected from the group consisting of: acetyl, imidazole, succinyl, and acyl.

29. (withdrawn) The composition of claim 24, wherein between 25% and 75% of the residues of the modified cationic polymer are modified.

30. (withdrawn) The composition of claim 29, wherein approximately 50% of the residues of the modified cationic polymer are modified.

31. (withdrawn) The composition of claim 23, wherein the RNAi-inducing entity comprises an siRNA.

32. (withdrawn) The composition of claim 23, wherein the RNAi-inducing entity comprises an shRNA.

33. (withdrawn) The composition of claim 23, wherein the RNAi-inducing entity comprises an RNAi-inducing vector.

34. (withdrawn) The composition of claim 23, wherein the RNAi-inducing entity comprises a DNA vector.

35. (withdrawn) The composition of claim 23, wherein the RNAi-inducing entity comprises a viral vector.

36. (withdrawn) The composition of claim 23, wherein the RNAi-inducing entity comprises a lentiviral vector.

37. (withdrawn) The composition of claim 23, wherein the RNAi-inducing entity comprises a lentivirus.

38. (currently amended) A method of inhibiting a target transcript associated with a respiratory disorder in a mammalian subject comprising ~~administering the~~ delivering a composition ~~of claim 23~~ comprising an RNAi-inducing entity and a delivery agent selected from the group consisting of cationic polymers and modified cationic polymers to the respiratory system of a subject by introducing the composition into the vascular system of the subject

wherein the RNAi-inducing entity is selected from an siRNA, an shRNA, and an RNAi-inducing vector whose presence within a cell results in production of an siRNA or shRNA; wherein the siRNA, shRNA or the siRNA or shRNA produced as a result of vector presence comprises a sequence that is complementary to a target transcript; and wherein the siRNA or shRNA; wherein the siRNA, shRNA or the siRNA or shRNA produced as a result of vector presence is at least 15 nucleotides in length.

39. (previously presented) The method of claim 49, wherein the solid organ is the lung.

40. (original) The method of claim 38, wherein the composition is administered by intravenous injection.

41. (original) The method of claim 38, wherein the composition is administered using a conventional fluid delivery technique.

42. (original) The method of claim 38, wherein the RNAi-inducing entity comprises an siRNA.

43. (withdrawn) The method of claim 38, wherein the RNAi-inducing entity comprises an shRNA.

44. (withdrawn) The method of claim 38, wherein the RNAi-inducing entity comprises an RNAi-inducing vector.

45. (withdrawn) The method of claim 38, wherein the RNAi-inducing vector comprises a DNA vector.

46. (withdrawn) The method of claim 38, wherein the RNAi-inducing vector comprises a viral vector.

47. (withdrawn) The method of claim 38, wherein the RNAi-inducing vector comprises a lentiviral vector.

48. (withdrawn) The method of claim 38, wherein the RNAi-inducing vector comprises a lentivirus.

49. (currently amended) A method of treating or preventing a respiratory disease or clinical condition associated with overexpression or inappropriate expression of a transcript or excessive functional activity of a polypeptide encoded by the transcript comprising the step of delivering [~~the~~] a composition [~~of claim 23~~] comprising a RNAi-inducing entity and a delivery agent selected from the group consisting of cationic polymers and modified cationic polymers to a respiratory system solid organ or tissue of a subject at risk of or suffering from the disease or clinical condition by introducing the composition into the vascular system of the subject;

wherein the RNAi-inducing entity is selected from an siRNA, an shRNA, and an RNAi-inducing vector whose presence within a cell results in production of an siRNA or shRNA; wherein the siRNA, shRNA or

the siRNA or shRNA produced as a result of vector presence comprises a sequence that is complementary to a target transcript; and wherein the siRNA, shRNA or the siRNA or shRNA produced as a result of vector presence is at least 15 nucleotides in length.

50. (withdrawn) The composition of claim 1, wherein the delivery agent comprises a surfactant suitable for introduction into the lung.

51. (withdrawn) The composition of claim 50, wherein the surfactant comprises 10-20% protein and 80-90% lipid by weight both based on the whole surfactant, which lipid consists of about 10% neutral lipid and of about 90% phospholipid.

52. (withdrawn) The composition of claim 50, wherein the surfactant is derived from animal tissue or lung lavage.

53. (withdrawn) The composition of claim 50, wherein the surfactant is synthetic.

54. (withdrawn) The composition of claim 50, wherein the surfactant is approved by the U.S. Food and Drug Administration.

55. (withdrawn) The composition of claim 50, wherein the surfactant is Infasurf.RTM., Survanta.RTM., or Exosurf.RTM..

56. (withdrawn) The composition of claim 50, wherein the RNAi-inducing entity comprises an siRNA

57. (withdrawn) The composition of claim 50, wherein the RNAi-inducing entity comprises an shRNA.

58. (withdrawn) The composition of claim 50, wherein the RNAi-inducing entity comprises an RNAi-inducing vector.

59. (withdrawn) The composition of claim 50, wherein the RNAi-inducing entity comprises a DNA vector.

60. (withdrawn) The composition of claim 50, wherein the RNAi-inducing entity comprises a viral vector.

61. (withdrawn) The composition of claim 50, wherein the RNAi-inducing entity comprises a lentiviral vector.

62. (withdrawn) The composition of claim 50, wherein the RNAi-inducing entity comprises a lentivirus.

63. (withdrawn) A method of inhibiting a target transcript in a mammalian subject comprising administering the composition of claim 50 to the respiratory system of a subject by inhalation or intranasal delivery.

64. (withdrawn) The method of claim 63, wherein the RNAi-inducing entity comprises an siRNA.

65. (withdrawn) The method of claim 63, wherein the RNAi-inducing entity comprises an shRNA.

66. (withdrawn) The method of claim 63, wherein the RNAi-inducing entity comprises an RNAi-inducing vector.

67. (withdrawn) The method of claim 63, wherein the RNAi-inducing entity comprises a viral vector.

68. (withdrawn) The method of claim 63, wherein the RNAi-inducing entity comprises a lentiviral vector.

69. (withdrawn) The method of claim 63, wherein the RNAi-inducing entity comprises a lentivirus.

70. (withdrawn) The method of claim 63, wherein the RNAi-inducing entity comprises a DNA vector.

71. (withdrawn) A method of treating or preventing a disease or clinical condition associated with overexpression or inappropriate expression of a target transcript or excessive functional activity of a polypeptide encoded by the target transcript comprising the step of administering the composition of claim 50 to the respiratory system of a subject at risk of or suffering from the disease or clinical condition by inhalation or intranasal delivery.

72. (withdrawn) The composition of claim 1, wherein the delivery agent is a peptide molecular transporter.

73. (withdrawn) The composition of claim 72, wherein the peptide molecular transporter is an arginine-rich peptide containing at least 4 arginine residues.

74. (withdrawn) The composition of claim 72, wherein the RNAi-inducing entity comprises an siRNA.

75. (withdrawn) The composition of claim 72, wherein the RNAi-inducing entity comprises an shRNA.

76. (withdrawn) The composition of claim 72, wherein the RNAi-inducing entity comprises an RNAi-inducing vector.

77. (withdrawn) The composition of claim 72, wherein the RNAi-inducing entity comprises a viral vector.

78. (withdrawn) The composition of claim 72, wherein the RNAi-inducing entity comprises a lentiviral vector.

79. (withdrawn) The composition of claim 72, wherein the RNAi-inducing entity comprises a lentivirus.

80. (withdrawn) The composition of claim 72, wherein the RNAi-inducing entity comprises a DNA vector.

81. (currently amended) A method of inhibiting expression of a target transcript of a respiratory virus in a mammalian subject comprising the step of administering to the subject a composition comprising: (i) an RNAI-inducing entity ~~an RNAi-inducing entity~~ targeted to the target transcript; and (ii) a delivery agent selected from the group consisting of: cationic polymers[[,]] and modified cationic polymers;

wherein the RNAi-inducing entity is selected from an siRNA, an shRNA, and an RNAi-inducing vector whose presence within a cell results in production of an siRNA or shRNA; wherein the siRNA, shRNA or the siRNA or shRNA produced as a result of vector presence comprises a sequence that is complementary to a target transcript; and wherein the siRNA, shRNA or the siRNA or shRNA produced as a result of vector presence is at least 15 nucleotides in length. ~~, peptide molecular transporters, surfactants suitable for introduction into the lung, lipids, liposomes, lipopolyplexes, non-cationic polymers, modified non-cationic polymers, bupivacaine, and chloroquine.~~

82. (previously presented) The method of claim 81, wherein administration of the composition inhibits expression of the target transcript in the lung.

83. (original) The method of claim 81, wherein administration of the composition inhibits expression of the target transcript in at least one tissue or organ other than the lung, in addition to, or instead of, inhibiting the transcript in the lung.

84. (currently amended) A method of treating or preventing a disease or condition associated with overexpression or inappropriate expression of a target transcript of a respiratory virus or inappropriate or excessive expression or activity of a polypeptide encoded by the transcript, the method comprising steps of: (a) providing a subject at risk of or suffering from a disease or condition associated with overexpression or inappropriate expression of a transcript of a respiratory virus or inappropriate or excessive expression or activity of a polypeptide encoded by the transcript; and (b) administering to the subject a composition comprising: (i) an RNAi-inducing entity targeted to the target transcript; and (ii) a delivery agent selected from the group consisting of: cationic polymers[[,]] and modified cationic polymers~~, peptide molecular transporters, surfactants suitable for introduction into the lung, lipids, liposomes, non-cationic polymers, modified non-cationic polymers, bupivacaine, and chloroquine~~

wherein the RNAi-inducing entity is selected from an siRNA, an shRNA, and an RNAi-inducing vector whose presence within a cell results in production of an siRNA or shRNA; wherein the siRNA, shRNA or the siRNA or shRNA produced as a result of vector presence comprises a sequence that is complementary to a target transcript; and wherein the siRNA, shRNA or the siRNA or shRNA produced as a result of vector presence is at least 15 nucleotides in length. ;.

85. (original) The method of claim 84, wherein the composition is administered by inhalation or intranasally.

86. (previously presented) The method of claim 85, wherein the composition is administered as an aerosol.

87. (original) The method of claim 84, wherein the composition is administered intravenously.

88. (original) The method of claim 87, wherein the composition is administered using a conventional

intravenous administration technique.

89. (original) The method of claim 84, wherein the delivery agent comprises a delivery enhancing moiety to enhance delivery to a cell of interest.

90. (original) The method of claim 89, wherein the delivery-enhancing moiety comprises an antibody, antibody fragment, or ligand that specifically binds to a molecule expressed by the cell of interest.

91-97. (canceled)

98. (previously presented) The method of claim 81, wherein the RNAi-inducing entity comprises a modified nucleotide.

99. (previously presented) The method of claim 84, wherein the RNAi-inducing entity comprises a modified nucleotide.